Sexual replication in the quasispecies model

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This paper develops a simplified model for sexual replication within the quasispecies formalism. We assume that the genomes of the replicating organisms are two-chromosomed and diploid, and that the fitness is determined by the number of chromosomes that are identical to a given master sequence. We also assume that there is a cost to sexual replication, given by a characteristic time τ_{seek} during which haploid cells seek out a mate with which to recombine. If the mating strategy is such that only viable haploids can mate, then when $\tau_{seek} = 0$, it is possible to show that sexual replication will always outcompete asexual replication. However, as τ_{seek} increases, sexual replication only becomes advantageous at progressively higher mutation rates. Once the time cost for sex reaches a critical threshold, the selective advantage for sexual replication disappears entirely. The results of this paper suggest that sexual replication is not advantageous in small populations per se, but rather in populations with low replication rates. In this regime, the cost for sex is sufficiently low that the selective advantage obtained through recombination leads to the dominance of the strategy. In fact, at a given replication rate and for a fixed environment volume, sexual replication is selected for in high populations because of the reduced time spent finding a reproductive partner.

Keywords: Sexual replication, diploid, haploid, quasispecies, error catastrophe, error cascade, survival of the flattest

I. INTRODUCTION

Sexual reproduction is the observed mode of reproduction for nearly all multicellular organisms. As such, the evolution of sex has been one of the central outstanding questions in evolutionary biology.

One of the biological explanations for the existence of sex is that it provides a natural mechanism for diploid organisms to eliminate deleterious mutations from a population [1]. The idea is that, by reproducing via a haploid intermediate, it is possible for haploids without defective genes to recombine with one another, thereby preventing the accumulation of deleterious mutations. Other explanations that have been advanced are that sex leads to greater variability in a population, making the population more adaptable in adverse conditions. It has also been postulated that sex evolved as a mechanism for coping with parasites [1].

In recent years, there have been a number of numerical studies focusing on the evolutionary dynamics of sexual replication [1, 2, 3, 4, 5]. These studies have established that, depending on the choice of parameters, either sexual or asexual modes of reproduction are the advantageous replication strategy. One study in particular argues that sexual reproduction is favored when the number of daughter genomes produced by the parents is high, since this reduces the amount of time required to find a reproductive partner [3].

In this paper, we present a relatively simple evolutionary dynamics model that allows us to compare sexual and asexual replication strategies. The model is analytically solvable, and treatable within the quasispecies formalism [6]. The essential result is that sexual replication is favored in populations with low replication rates, and when the characteristic time associated with finding a reproductive partner is small compared with the time scale associated with replication. These results suggest that increasing population density favors the sexual replication strategy, since it reduces the time scale associated with finding a mate.

This paper is organized as follows: In the following section (Section II), we develop a simplified model for sexual replication, whose steady-state behavior we proceed to characterize in Section III. In Section IV we compare sexual and asexual replication, and establish regimes where each is the preferred mode of reproduction. We conclude the paper in Section V with a brief discussion and an outline of avenues for future research.

II. A SIMPLIFIED MODEL FOR SEXUAL REPLICATION

In a simplified model for sexual replication, we assume that we have a population of single-celled organisms, where each organism has a genome consisting of two chromosomes. We assume that each chromosome may be denoted by a linear symbol sequence $\sigma = s_1 \dots s_L$, where each letter, or base, s_i, is chosen from an alphabet of size S ($= 4$ for terrestrial life). We further assume that there exists a "master" sequence σ_0 for which a given chromosome is functional. It is assumed that a chromosome is nonfunctional whenever $\sigma \neq \sigma_0$ (that is, the genes on such a chromosome are defective).

Within this approximation, there are three distinct types of genomes in the population: (1) $\{\sigma_0, \sigma_0\}$ – Genomes where both chromosomes are identical to the "master" sequence. (2) $\{\sigma_0, \sigma \neq \sigma_0\}$ – Genomes where only one of the chromosomes is identical to the "master" sequence, while the other chromosome is defective. (3)

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$\{\sigma \neq \sigma_0, \sigma' \neq \sigma_0\}$ – Genomes where both of the chromosomes are defective.

We are therefore dealing with a diploid population. If we assign the gene sequence σ_0 as *Viable*, while all other gene sequences are *Unviable*, then our three genome types may be classified as $\{V, V\}$, $\{V, U\}$, and $\{U, U\}$, where V/U stand for Viable/Unviable.

We assume that the organisms replicate with a first-order growth rate constant. For the three distinct genome types, the first-order growth rate constants are taken to be κ_{VV}, κ_{VU}, and κ_{UU}. We have that $\kappa_{VV} \geq \kappa_{VU} > \kappa_{UU}$.

The sexual replication of the population occurs as follows: The diploid organisms divide to form a population of haploid organisms. It is assumed that those haploid organisms containing a genome of type U are incapable of participating further in the reproductive process, so that only viable haploids can recombine with each other. The newly formed diploids then divide via the normal mitotic pathways to form two new daughter cells.

To develop a set of ordinary differential equations governing the replication dynamics described above, we first let n_{VV} denote the total number of organisms with genome of type $\{V, V\}$, n_{VU} denote the total number of organisms with genome of type $\{V, U\}$, and n_{UU} denote the total number of organisms with genome of type $\{U, U\}$. We also let n_V denote the population of viable haploids. We then wish to obtain expressions for dn_{VV}/dt, dn_{VU}/dt, dn_{UU}/dt, and dn_V/dt.

First note that, the diploid to haploid division leads to destruction of each of the diploid genomes at a rate given by $-\kappa_{VV} n_{VV}$ for $\{V, V\}$, and similarly for the other genomes, and a creation of viable haploid genomes at a rate given by $2\kappa_{VV} n_{VV} + \kappa_{VU} n_{VU}$.

If we let τ_{seek} denote the average amount of time a viable haploid spends searching for a viable haploid mate, then in a given amount of time dt the total number of viable haploids who have recombined is given by $n_V dt/\tau_{seek}$ (the individual times are Poisson distributed). Therefore, recombination leads to a destruction rate of haploids given by n_V/τ_{seek}, and a creation rate of diploids given by $(1/2)n_V/\tau_{seek}$.

If we let p denote the probability of correctly replicating a chromosome, then neglecting backmutations we have that $V \to V$ with probability p, $V \to U$ with probability $1-p$, and $U \to U$ with probability 1. Using this, we can construct the various possible replication pathways and their associated probabilities, illustrated in Figure 2. From these pathways, we can construct the contribution to n_{VV}, n_{VU}, and n_{UU} in turn.

For n_{VV}, all three replication pathways in Figure 1 give a contribution. Taking into account probabilities and degeneracies, we have a total contribution of $2p^2$ from the first pathway, $2p(1-p)$ from the second pathway, and $(1-p)^2/2$ from the second pathway, giving a total rate of production of $(1/2)n_V/\tau_{seek} \times [2p^2 + 2p(1-p) + (1-p)^2/2] = (1/4)n_V/\tau_{seek}(1+p)^2$.

For n_{VU}, similar reasoning gives a rate of production of $(1/2)n_V/\tau_{seek} \times [2p(1-p) + 2(1-p)^2/2] = (1/2)n_V \tau_{seek}(1-p^2)$.

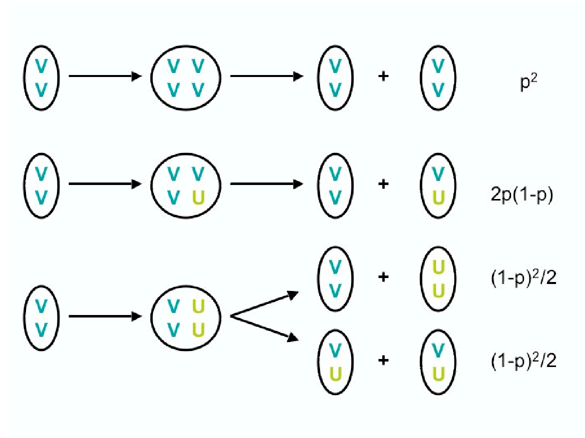

FIG. 1: The various replication pathways and their associated probabilities. The factor of 2 in the second pathway comes from the fact that either the top or bottom parent "V" chromosome can form a daughter "U" chromosome.

For n_{UU}, we obtain $(1/2)n_V/\tau_{seek} \times (1-p)^2/2 = (1/4)n_V/\tau_{seek}(1-p)^2$.

Putting everything together, we obtain the system of differential equations,

$$\begin{aligned}
\frac{dn_{VV}}{dt} &= -\kappa_{VV} n_{VV} + \frac{n_V}{4\tau_{seek}}(1+p)^2 \\
\frac{dn_{VU}}{dt} &= -\kappa_{VU} n_{VU} + \frac{n_V}{2\tau_{seek}}(1-p^2) \\
\frac{dn_{UU}}{dt} &= -\kappa_{UU} n_{UU} + \frac{n_V}{4\tau_{seek}}(1-p)^2 \\
\frac{dn_V}{dt} &= 2\kappa_{VV} n_{VV} + \kappa_{VU} n_{VU} - \frac{n_V}{\tau_{seek}}
\end{aligned} \tag{1}$$

We can non-dimensionalize these equations by defining $\tau = t/\tau_{seek}$, and $\tilde{\kappa}_{VV} = \kappa_{VV}\tau_{seek}$, $\tilde{\kappa}_{VU} = \kappa_{VU}\tau_{seek}$, $\tilde{\kappa}_{UU} = \kappa_{UU}\tau_{seek}$. Then we obtain,

$$\begin{aligned}
\frac{dn_{VV}}{d\tau} &= -\tilde{\kappa}_{VV} n_{VV} + \frac{n_V}{4}(1+p)^2 \\
\frac{dn_{VU}}{d\tau} &= -\tilde{\kappa}_{VU} n_{VU} + \frac{n_V}{2}(1-p^2) \\
\frac{dn_V}{dt} &= 2\tilde{\kappa}_{VV} n_{VV} + \tilde{\kappa}_{VU} n_{VU} - n_V
\end{aligned} \tag{2}$$

Define $n = n_{VV} + n_{VU} + n_{UU} + n_V$, $n' = n_{VV} + n_{VU} + n_{UU}$, $x_{VV} = n_{VV}/n$, $x'_{VV} = n_{VV}/n'$, $x_{VU} = n_{VU}/n$, $x'_{VU} = n_{VU}/n'$, $x_{UU} = n_{UU}/n$, $x'_{UU} = n_{UU}/n'$, $x_V = n_V/n$. Note that $x'_{VV} = x_{VV}/(1-x_V)$, $x'_{VU} = x_{VU}/(1-x_V)$, $x'_{UU} = x_{UU}/(1-x_V)$, and $n_V/n' = x_V/(1-x_V)$.

Then defining $\bar{\kappa}(\tau) = (1/n)dn/d\tau$, $\bar{\kappa}(\tau)' = (1/n')dn'/d\tau$, we have,

$$\begin{aligned}
&\bar{\kappa}(\tau) = \tilde{\kappa}_{VV} x_{VV} - \tilde{\kappa}_{UU} x_{UU} \\
&\bar{\kappa}(\tau)' = -(\tilde{\kappa}_{VV} x'_{VV} + \tilde{\kappa}_{VU} x'_{VU} + \tilde{\kappa}_{UU} x'_{UU}) \\
&+ \frac{x_V}{1-x_V}
\end{aligned} \tag{3}$$

Re-expressing the dynamical equations in terms of the x_{VV}, x_{VU}, x_{UU}, x_V population fractions, we have,

$$\begin{aligned}\frac{dx_{VV}}{d\tau} &= -(\tilde{\kappa}_{VV} + \bar{\kappa}(\tau))x_{VV} + \frac{x_V}{4}(1+p)^2 \\ \frac{dx_{VU}}{d\tau} &= -(\tilde{\kappa}_{VU} + \bar{\kappa}(\tau))x_{VU} + \frac{x_V}{2}(1-p^2) \\ \frac{dx_{UU}}{d\tau} &= -(\tilde{\kappa}_{UU} + \bar{\kappa}(\tau))x_{UU} + \frac{x_V}{4}(1-p)^2 \\ \frac{dx_V}{d\tau} &= -(1+\bar{\kappa}(\tau))x_V + 2\tilde{\kappa}_{VV}x_{VV} + \tilde{\kappa}_{VU}x_{VU}\end{aligned} \tag{4}$$

III. EQUILIBRIUM MEAN FITNESS RESULTS

At steady-state, the above time derivatives may all be set to 0, giving,

$$x_V = \frac{2\tilde{\kappa}_{VV}x_{VV} + \tilde{\kappa}_{VU}x_{VU}}{1+\bar{\kappa}(\tau=\infty)} \tag{5}$$

Therefore, at steady-state, we have that,

$$\begin{aligned}\bar{\kappa}(\tau=\infty)' &= -\frac{1}{1-x_V}[((2\tilde{\kappa}_{VV}x_{VV} + \tilde{\kappa}_{VU}x_{VU}) \\ &\quad -(\tilde{\kappa}_{VV}x_{VV} - \tilde{\kappa}_{UU}x_{UU})] + \frac{x_V}{1-x_V} \\ &= \frac{1}{1-x_V}[x_V + \bar{\kappa}(\tau=\infty) - x_V(1+\bar{\kappa}(\tau=\infty))] \\ &= \bar{\kappa}(\tau=\infty)\end{aligned} \tag{6}$$

and so it is equivalent to measure the mean fitness of the population at steady-state using either $\bar{\kappa}(\tau)$ and $\bar{\kappa}(\tau)'$. This is important, because, in comparing mean fitness results with an asexually replicating population, the natural mean fitness result to use is $\bar{\kappa}(\tau)'$. The equivalence between $\bar{\kappa}(\tau)$ and $\bar{\kappa}(\tau)'$ means that we can compute $\bar{\kappa}(\tau)$ at steady-state and compare the results directly with the value of $\bar{\kappa}(\tau)$ for the asexually replicating population.

Plugging the steady-state value of x_V into the steady-state equations for x_{VV} and x_{VU}, we obtain,

$$\begin{aligned}0 &= [\tilde{\kappa}_{VV}(2(\frac{1+p}{2})^2\frac{1}{1+\bar{\kappa}(\tau=\infty)} - 1) - \bar{\kappa}(\tau=\infty)]x_{VV} \\ &\quad +\frac{1}{4}(1+p)^2\frac{\tilde{\kappa}_{VU}x_{VU}}{1+\bar{\kappa}(\tau=\infty)} \\ 0 &= [\tilde{\kappa}_{VU}(\frac{1}{2}(1-p^2)\frac{1}{1+\bar{\kappa}(\tau=\infty)} - 1) - \bar{\kappa}(\tau=\infty)]x_{VU} \\ &\quad +(1-p^2)\frac{1}{1+\bar{\kappa}(\tau)}\tilde{\kappa}_{VV}x_{VV}\end{aligned} \tag{7}$$

We can solve the first equation for x_{VU} in terms of x_{VV}. Plugging the resulting expression into the second equation, we obtain, after some algebra, the quadratic,

$$\begin{aligned}0 &= \bar{\kappa}(\tau=\infty)^2 \\ &\quad -[\tilde{\kappa}'_{VV}(2(\frac{1+p}{2})^2 - 1) - \frac{1}{2}\tilde{\kappa}'_{VU}(1+p^2)]\bar{\kappa}(\tau=\infty) \\ &\quad -\tilde{\kappa}'_{VV}\tilde{\kappa}'_{VU}p\end{aligned} \tag{8}$$

where $\tilde{\kappa}'_{VV} \equiv \tilde{\kappa}_{VV}/(1+\tilde{\kappa}_{VV})$, $\tilde{\kappa}'_{VU} \equiv \tilde{\kappa}_{VU}/(1+\tilde{\kappa}_{VU})$.

We can further simplify the notation by defining $\kappa = \tilde{\kappa}_{VV}$, and $\alpha = \tilde{\kappa}_{VU}/\tilde{\kappa}_{VV}$. Then $\bar{\kappa}(\tau=\infty)/\kappa$ is the solution to the quadratic,

$$0 = x^2 - A(p,\kappa,\alpha)x - B(p,\kappa,\alpha) \tag{9}$$

where,

$$\begin{aligned}A(p,\kappa,\alpha) &= \frac{1}{1+\kappa}[2(\frac{1+p}{2})^2 - 1] - \frac{1}{2}\frac{\alpha}{1+\alpha\kappa}(1+p^2) \\ B(p,\kappa,\alpha) &= \frac{1}{1+\kappa}\frac{\alpha}{1+\alpha\kappa}p\end{aligned} \tag{10}$$

Differentiating both sides of the quadratic, it is possible to show, after some manipulation, that $dx/dp > 0$, and hence that the mean fitness is an increasing function of p.

IV. COMPARISON OF SEXUAL AND ASEXUAL REPLICATION

If, for simplicity, we assume that $\kappa_{UU} = 0$, then for asexual replication the steady-state value for $\bar{\kappa}(\tau=\infty)/\kappa$ may be readily characterized [7]: It is given by $\max\{2(\frac{1+p}{2})^2 - 1, \alpha p\}$. Therefore, if p_{crit} is defined by the equality $2((1+p_{crit})/2)^2 - 1 = \alpha p_{crit}$, then,

$$\frac{\bar{\kappa}(\tau=\infty)}{\kappa} = \begin{cases} 2(\frac{1+p}{2})^2 - 1 & \text{if } p \in [p_{crit}, 1] \\ \alpha p & \text{if } p \in (0, p_{crit}] \end{cases} \tag{11}$$

We can compare these values with that obtained for sexual replication.

A. Case 1: $\kappa = 0$

We begin by considering the case where there is no time cost associated with sex, so that $\tau_{seek} = 0 \Rightarrow \kappa = 0$. Then

$$\begin{aligned}A(p,0,\alpha) &= [2(\frac{1+p}{2})^2 - 1] - \frac{1}{2}\alpha(1+p^2) \\ B(p,0,\alpha) &= \alpha p\end{aligned} \tag{12}$$

We claim that for $\kappa = 0$, $\bar{\kappa}(\tau=\infty)/\kappa \geq \max\{2(\frac{1+p}{2})^2 - 1, \alpha p\}$, with equality occurring only when $p = 1$ for arbitrary α, and $\alpha = 0, 1$.

To prove this claim, note first that for $p = 1$, we have $2(\frac{1+p}{2})^2 - 1 = 1$, and that $\bar{\kappa}(\tau=\infty)/\kappa = 1 = \max\{1, \alpha\}$. So since the claim is true for $p = 1$, we may now consider $p \in [0, 1)$.

If $\alpha = 0$, then $\bar{\kappa}(\tau=\infty) = \max\{2(\frac{1+p}{2})^2 - 1, 0\}$, while if $\alpha = 1$, then $\bar{\kappa}(\tau=\infty) = p = \max\{2(\frac{1+p}{2})^2 - 1, p\}$, since $2(\frac{1+p}{2})^2 - 1 \leq p$ for $p \in [0, 1]$, with equality occuring only when $p = 1$.

So, we now consider the case where $\alpha \in (0, 1)$, and $p \in [0, 1)$. If we define $k(p) = 2(\frac{1+p}{2})^2 - 1$, then we

have two possibilities: Either $\max\{k(p), \alpha p\} = k(p)$, or $\max\{k(p), \alpha p\} = \alpha p$. We will consider each of these two cases in turn.

So, first assume that $\max\{k(p), \alpha p\} = k(p)$. We wish to show that,

$$\frac{1}{2}[k(p) - \frac{1}{2}\alpha(1+p^2) + \sqrt{(k(p) - \frac{1}{2}\alpha(1+p^2))^2 + 4\alpha p}] > k(p) \tag{13}$$

After some manipulation, we obtain that this condition is equivalent to the condition that

$$0 > p^4 + 2p^3 - 2p - 1 \tag{14}$$

To establish this inequality for $p \in [0, 1)$, note that $p^4 + 2p^3 - 2p - 1 = (p-1)(p^3 + 3p^2 + 3p + 1)$. Since $p^3 + 3p^2 + 3p + 1 > 0$ for $p \in [0, 1)$, and since $p - 1 < 0$ for $p \in [0, 1)$, the inequality follows.

So now suppose that $\max\{k(p), \alpha p\} = \alpha p$, so that $k(p) < \alpha p$. Then for our calculations, we first re-write $A(p, 0, \alpha)$ as $\alpha(p-1) + (1-\alpha)k(p)$. Then we wish to show that,

$$\begin{aligned} &\frac{1}{2}[\alpha(p-1) + (1-\alpha)k(p) + \\ &\sqrt{(\alpha(p-1) + (1-\alpha)k(p))^2 + 4\alpha p}] \\ &> \alpha p \end{aligned} \tag{15}$$

After some manipulation, this becomes equivalent to the condition that,

$$k(p) + 1 > \alpha(k(p) + 1) \tag{16}$$

which is certainly true, since $k(p) + 1 > 0$ for $p \in [0, 1)$, and $\alpha \in (0, 1)$ by assumption.

Therefore, we have proven our claim, and hence, within this model, sexual replication leads to a greater mean fitness for a population than asexual replication, assuming that there is no cost associated with sex. Figure 2 shows a plot of $\bar{\kappa}(\tau = \infty)/\kappa$ for both sexual and asexual replication, assuming $\alpha = 1/2$ and $\kappa = 0$.

Note that for $\kappa = 0$, if a sexually and asexually replicating population were placed in an identical flask, then under the circumstances dictated by our model the sexually replicating population would eventually dominate the population (that is, the fraction of sexually replicating organisms would increase to 1, while the fraction of asexually replicating organisms would decrease to 0).

B. Case 2: $\kappa > 0$

For $\kappa > 0$, we have, for sexual replication, that $\bar{\kappa}(\tau = \infty)/\kappa = \frac{1}{1+\kappa}$ for $p = 1$. Since for asexual replication we get $\bar{\kappa}(\tau = \infty)/\kappa = 1$ for $p = 1$, it follows by continuity that there exists a regime $[p_=(\kappa), 1]$ for which asexual reproduction leads to a greater mean fitness of the population than sexual reproduction. Presumably, as κ increases, $p_=(\kappa)$ should decrease.

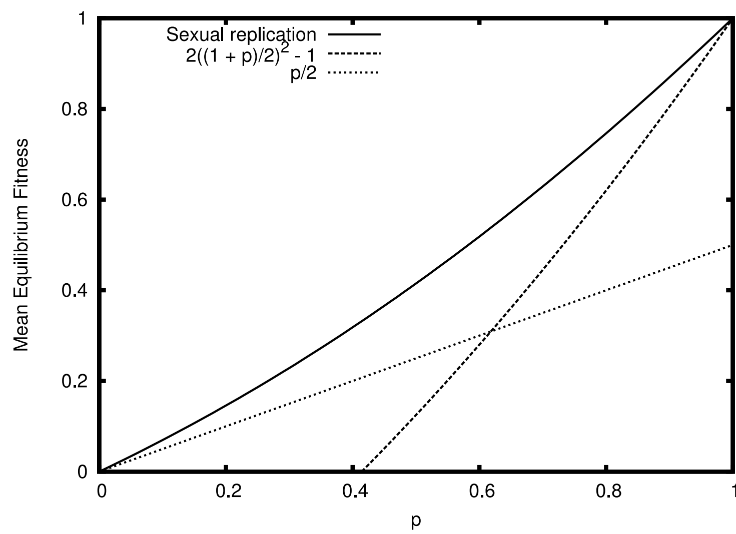

FIG. 2: Comparison of $\bar{\kappa}(\tau = \infty)/\kappa$ for both sexual and asexual replication, with $\kappa = 0$ and $\alpha = 1/2$. Note that sexual replication outcompetes asexual replication for all mutation regimes.

We can determine, for a given κ, the mutation regime where asexual replication outcompetes sexual replication, and the mutation regime where sexual replication outcompetes asexual replication. To do this, we do not attempt to compute $p_=(\kappa)$ directly. Rather, as a function of p, we seek to determine $\kappa_=(p)$, the value of κ for which asexual and sexual replication yield identical mean fitnesses. Since by definition $\kappa_=(p(\kappa)) = \kappa$, the function $\kappa_=(p)$ may be inverted to obtain $p_=(\kappa)$. In what follows, we restrict our analysis to the case where $\alpha \in (0, 1)$ (if $\alpha = 0, 1$, then for $\kappa > 0$ asexual reproduction outcompetes sexual reproduction for all values of p).

Because the mean fitness of an asexually replicating population falls into two distinct regimes defined by the cutoff p_{crit} (at least, within the context of our model), we must determine $\kappa_=(p)$ separately for $p \leq p_{crit}$ and $p > p_{crit}$. For $p \leq p_{crit}$, we have for asexual replication that $\bar{\kappa}(\tau = \infty)/\kappa = \alpha p$, and hence we must have,

$$\begin{aligned} 0 &= (\alpha p)^2 - (\frac{1}{1+\kappa_=}k(p) - \frac{1}{2}\frac{\alpha}{1+\alpha\kappa_=}(1+p^2))(\alpha p) \\ &- \frac{1}{1+\kappa_=}\frac{1}{1+\alpha\kappa_=}(\alpha p) \end{aligned} \tag{17}$$

Assuming that $\alpha p > 0$, this expression may be rearranged and simplified to,

$$0 = (\alpha\kappa_=)^2 p + (\alpha p + 1)(\alpha\kappa_=) - \frac{1}{2}(1-\alpha)(1+p)^2 \tag{18}$$

so that $\alpha\kappa_=$, and hence $\kappa_=$, may be solved using the quadratic formula.

We claim that $\kappa_=$ is an increasing function of p on the interval $[0, p_{crit}]$. We can prove this by showing that

$\alpha\kappa_=$ is an increasing function of p on the interval $[0, p_{crit}]$. Defining $x(p) = \alpha\kappa_=(p)$, we have,

$$0 = px(p)^2 + (\alpha p + 1)x(p) - \frac{1}{2}(1-\alpha)(1+p)^2 \qquad (19)$$

Differentiating with respect to p, we obtain,

$$0 = (2px(p) + \alpha p + 1)x'(p) + x(p)^2 + \alpha x(p) - (1-\alpha)(1+p) \qquad (20)$$

so we wish to show that $x(p)^2 + \alpha x(p) - (1-\alpha)(1+p) < 0$ for $p \in (0, p_{crit})$. Multiplying both sides of the inequality by p, and noting that $px(p)^2 = \frac{1}{2}(1-\alpha)(1+p)^2 - (\alpha p + 1)x(p)$, we have that for $p > 0$ we need to establish the inequality,

$$x(p) > \frac{1}{2}(1-\alpha)(1-p^2) \qquad (21)$$

To prove this inequality, note first that $x(0) = \frac{1}{2}(1-\alpha)$, and $x'(0) = \frac{1}{4}(1-\alpha)(3-\alpha) > 0$. By continuity, $x'(p) > 0$ in a neighborhood of $p = 0$. If $x'(p) \leq 0$ for some $p > 0$, then by the Intermediate Value Theorem there exists at least one $p > 0$ for which $x'(p) = 0$. If $p^* \equiv \inf\{p \in [0,1] | x'(p) = 0\}$, then by continuity it follows that $x'(p^*) = 0$, and hence $p^* > 0$. Therefore, $x'(p) > 0$ for $p \in [0, p^*)$, otherwise by the Intermediate Value Theorem there would exist a $p^{**} < p^*$ such that $x'(p^{**}) = 0$, contradicting the definition of p^*. But, since $x'(p) > 0$ for $p \in [0, p^*)$, it follows that $x(p)$ is increasing on $[0, p^*]$, hence $x(p^*) > x(0) = \frac{1}{2}(1-\alpha) > \frac{1}{2}(1-\alpha)(1-(p^*)^2)$, which implies that $x'(p^*) > 0 \Rightarrow\Leftarrow$. Therefore, $x'(p) > 0$ for $p \in [0,1]$, hence on $[0, p_{crit}]$, $\kappa_=(p)$ increases from $\frac{1}{2}(1-\alpha)/\alpha$ to $\kappa_=(p_{crit}(\alpha))$.

Now, for $p \in [p_{crit}, 1]$, we have for an asexually replicating population that $\bar{\kappa}(\tau = \infty)/\kappa = k(p)$, hence, in this regime, $\kappa_=(p)$ is defined by,

$$\begin{aligned} 0 &= k(p)^2 - (\frac{1}{1+\kappa_=}k(p) - \frac{1}{2}\frac{\alpha}{1+\alpha\kappa_=}(1+p^2))k(p) \\ &\quad - \frac{1}{1+\kappa_=}\frac{\alpha}{1+\alpha\kappa_=}p \end{aligned} \qquad (22)$$

which after some manipulation may be re-arranged to give,

$$0 = \kappa_=^2 + B(p,\alpha)\kappa_= - C(p,\alpha) \qquad (23)$$

where $B(p,\alpha) \equiv 1 + 1/\alpha + (1-p)/k(p)$, $C(p,\alpha) \equiv \frac{1}{2}\frac{1}{k(p)}(1 + 1/k(p))(1-p^2)$. We then have that,

$$\kappa_=(p) = B(\sqrt{1 + 4\frac{C}{B^2}} - 1) \qquad (24)$$

We claim that $\kappa_=(p)$ is a decreasing function of p for $p \in [p_{crit}, 1]$. We will prove this by showing that B and C/B^2 are both decreasing functions of p for $p \in [p_{crit}, 1]$.

To prove that B is a decreasing function of p for $p \in [p_{crit}, 1]$, we need show that $(1-p)/k(p)$ is a decreasing function of p for $p \in [p_{crit}, 1]$. Differentiating, we obtain,

$$\frac{d}{dp}(\frac{1-p}{k(p)}) = -\frac{1}{2}\frac{1-p^2+2p}{k(p)^2} < 0 \qquad (25)$$

so B is certainly a decreasing function of p for $p \in [p_{crit}, 1]$.

Now, after some manipulation, we can show that,

$$\frac{C}{B^2} = \frac{1}{2}\alpha^2 \frac{1-p^2}{(1+k(p))(1+\alpha - \frac{1+\alpha p}{1+k(p)})^2} \qquad (26)$$

Note that $1-p^2$ is decreasing for $p \in [p_{crit}, 1]$, and that $1 + k(p)$ is increasing. We also have that,

$$\frac{d}{dp}(\frac{1+\alpha p}{1+k(p)}) = -\frac{(\alpha/2)p^2 + p + (1-\alpha/2)}{(1+k(p))^2} < 0 \qquad (27)$$

so that $(1+\alpha p)/(1+k(p))$ is a decreasing function of p. Therefore, $1 + \alpha - (1+\alpha p)/(1+k(p))$ is an increasing function of p, hence C/B^2 is decreasing for $p \in [p_{crit}, 1]$, as we wished to show.

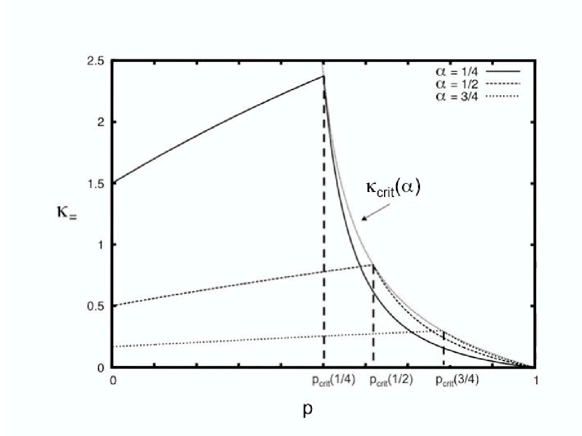

FIG. 3: $\kappa_=$ versus p for $\alpha = 1/4, 1/2, 3/4$. A graph of $\kappa_{crit}(\alpha)$ is included as well.

Figure 3 illustrates the behavior of $\kappa_=(p)$ for three values of α.

In what follows, we shall change our notation slightly to explicitly indicate that $\kappa_=$ also depends on α. Thus, we shall re-denote $\kappa_=(p)$ by $\kappa_=(p,\alpha)$. This notation was not needed in the previous arguments, since we were considering the behavior of $\kappa_=$ at a fixed α.

We may now summarize the behavior of $\kappa_=(p,\alpha)$ as a function of p:

From 0 to p_{crit}, $\kappa_=(p,\alpha)$ increases from $\frac{1}{2}(1-\alpha)/\alpha$ to $\kappa_{crit}(\alpha) \equiv \kappa_=(p_{crit}(\alpha), \alpha)$, while from p_{crit} to 1, $\kappa_=(p,\alpha)$ decreases from $\kappa_{crit}(\alpha)$ to 0. This behavior leads to three distinct regimes of κ.

For $\kappa \in [0, \frac{1}{2}(1-\alpha)/\alpha]$, there exists only one value of p for which asexual and sexual replication yield identical mean fitness results. This value of p is contained in the interval $[p_{crit}, 1]$. As κ increases from 0 to $\frac{1}{2}(1-\alpha)/\alpha$,

this value of p decreases. For these values of κ, asexual replication is advantageous over sexual replication at low mutation rates. However, there is a crossover replication fidelity where sexual replication becomes advantageous. As κ increases, this crossover replication fidelity gets pushed to lower values. This makes sense, since a higher value of κ corresponds to a greater penalty associated with sex.

For $\kappa \in [\frac{1}{2}(1-\alpha)/\alpha, \kappa_{crit}(\alpha)]$, there exist exactly two values of p for which asexual and sexual replication yield identical mean fitness results. One value of p is contained in the interval $[0, p_{crit}]$, while the other value is contained in the interval $[p_{crit}, 1]$. As κ increases from $\frac{1}{2}(1-\alpha)/\alpha$ to $\kappa_{crit}(\alpha)$, the value of p in $[0, p_{crit}]$ increases from 0 to $p_{crit}(\alpha)$, while the value of p in $[p_{crit}, 1]$ decreases to $p_{crit}(\alpha)$. For these values of κ, asexual replication is also advantageous over sexual replication at low mutation rates. As with the previous regime, there is a crossover replication fidelity where sexual replication becomes advantageous. However, in contrast to the first κ regime, there is a second crossover replication fidelity where asexual replication again becomes advantageous. For these values of κ, the cost associated with sex is still sufficiently low that sexual replication can become the advantageous strategy at higher mutation rates. However, the cost of sex is sufficiently high that, at even higher mutation rates, sexual recombination no longer offsets the production of unviable chromosomes from viable ones to an extent that makes the strategy advantageous.

Finally, for $\kappa \in (\kappa_{crit}(\alpha), \infty)$, the cost associated with sex is so high that sexual replication is never the advantageous strategy.

As a final note for this subsection, we can show that $\kappa_{crit}(\alpha)$ is a decreasing function of α. Differentiating the quadratic equation given by Eq. (19) with respect to α (where $x = x(\alpha) \equiv \alpha\kappa_{crit}(\alpha)$), we have,

$$\begin{aligned} 0 &= (2xp_{crit} + \alpha p_{crit} + 1)\frac{dx}{d\alpha} \\ & (x^2 + \alpha x - (1-\alpha)(1+p_{crit}))\frac{dp_{crit}}{d\alpha} \\ & + p_{crit}x + \frac{1}{2}(1+p_{crit})^2 \end{aligned} \tag{28}$$

Differentiating both sides of the equality defining p_{crit}, it is possible to show that $dp_{crit}/d\alpha = p_{crit}/(1-\alpha+p_{crit})$. We also have, from a previous analysis, that $px^2 + \alpha xp - (1-\alpha)p(1+p) = \frac{1}{2}(1-\alpha)(1-p^2) - x$, so that, to show $dx/d\alpha < 0$, we need to show that

$$0 < \frac{\frac{1}{2}(1-\alpha)(1-p_{crit}^2) - x}{1-\alpha+p_{crit}} + p_{crit}x + \frac{1}{2}(1+p_{crit})^2 \tag{29}$$

Multiplying by $1-\alpha+p_{crit}$ and simplifying, this is equivalent to the inequality,

$$0 < (1-\alpha-x) + p_{crit}[(1-\alpha)(1+x) + xp_{crit} + \frac{1}{2}(1+p_{crit})^2] \tag{30}$$

Since we showed that the expression for $x(p)$ in Eq. (19), valid over $p \in [0, p_{crit}]$, is an increasing function of p for $p \in [0,1]$, then solving the quadratic in Eq. (19) for $p = 1$ gives $x \leq 1-\alpha$. Therefore, $1-\alpha-x \geq 0$, hence the inequality holds.

We have therefore shown that $\alpha\kappa_{crit}(\alpha)$ is a decreasing function of α, hence $\kappa_{crit}(\alpha)$ is a decreasing function of α. When $\alpha = 1$, $p_{crit} = 1$, so $\kappa_= = 0$. As $\alpha \to 0$, $p_{crit} \to \sqrt{2}-1$, so $\alpha\kappa_= \to (\sqrt{4\sqrt{2}-3}-1)/[2(\sqrt{2}-1)] \Rightarrow \kappa_= \to \infty$.

C. Consideration of $\kappa_{UU} > 0$

When $\kappa_{UU} > 0$, the results for sexual replication remain unchanged. However, the results for asexual replication change somewhat, since now an additional localization to delocalization transition can occur, once $\kappa_{UU} = \max\{\kappa_{VV}(2((1+p)^2/2)-1), \kappa_{VU}p, \kappa_{UU}\}$. It is therefore possible to have a situation where sexual replication only becomes advantageous once the mean fitness of an asexually replicating population is κ_{UU}. With an appropriate choice of parameters, it is then possible that the mean fitness of the sexually replicating population is less than κ_{UU}, so that sexual replication will never be the preferred replication strategy. We leave the investigation of this phenomenon for future work.

In any event, for $\kappa_{UU} > 0$, asexual replication will become the advantageous mode of replication at sufficiently high mutation rates, since the mean fitness of the sexually replicating population decreases to zero, while after complete delocalization over the genome space has occurred, the mean fitness of the asexually replicating population becomes κ_{UU}. This result, however, is likely due to a mating strategy that essentially "throws away" the "U" chromosomes. Other mating strategies, where all haploids are capable of mating, may not exhibit the same effect.

V. DISCUSSION, CONCLUSIONS, AND FUTURE RESEARCH DIRECTIONS

This paper developed a simplified model for sexual replication, and showed, within the context of the model, that a sexually replicating population will outcompete an asexually replicating one when there there is no cost associated with sex. We further showed that if the cost associated with sex is sufficiently low, then sexual replication becomes advantageous at higher mutation rates, because recombination prevents the accumulation of defective mutations in the diploid genomes (assuming that there is a fitness penalty associated with the defective mutations). The cost for sex was measured by the dimensionless parameter κ, defined to be the product of the first-order growth rate constant of the mutation-free genomes (κ_{VV}), and the characteristic time associated with finding a recombination partner (τ_{seek}). Since

$\kappa_{VV} = 1/\tau_{rep}$, where τ_{rep} denotes a characteristic replication time, it follows that $\kappa = \tau_{seek}/\tau_{rep}$. Therefore, the cost associated with sex is measured by the ratio of the time a haploid spends finding a recombination partner with the time scale for replication. The smaller this ratio, the smaller the fitness penalty incurred by reproducing via a haploid intermediate, and the greater the selective advantage for sex.

The implications of this model are that sexual replication is favored in environments where organisms replicate relatively slowly, and in environments where the time spent finding a recombination partner is small compared with the time scale for replication. Thus, sexual replication is favored in environments with high population density. These results are therefore consistent with the observation that sexual replication is the preferred (and generally the only) mode of reproduction for nearly all multicellular organisms.

That sexual replication only becomes the preferred mode of reproduction at low κ suggests why sexual replication occurs as a stress response in some organisms, such as *Saccharomyces cerevisiae* (Baker's yeast). When conditions are favorable, κ_{VV}, and hence κ, are relatively high, so asexual replication is the advantageous strategy. Under sufficiently adverse conditions, κ can drop to levels where the sexual strategy becomes advantageous. The replicative strategy that can adopt the optimal replication strategy for the given environment will have a selective advantage (assuming that resource costs for maintaining this switching behavior are not prohibitive), and so organisms carrying this strategy in their genomes will dominate the population.

However, as one moves toward more complex life forms, the replication rate drops to values such that asexual replication is almost never the preferred mode of reproduction, so that the ability for an organism to switch between the two modes of reproduction disappears. At this point, we postulate that the division of haploid cells into two distinct types of gametes, and then later the division of the organisms themselves into male and female, are the result of selection for evolutionary pathways leading to the division of labor and specialization of tasks associated with sexual replication. When replication rates are low, and when the time cost associated with sex is low, then it is likely more efficient (in terms of resource utilization) to divide the reproductive tasks associated with sexual replication among two types of organisms ("male" and "female"). The relative fitness advantage as a result of such savings in resource costs likely increases with the complexity of the organism, leading to a stronger selection pressure for a male-female split as organismal complexity grows.

In this paper, we assumed that only haploid cells with viable chromosomes are capable of engaging in sexual recombination. This allowed a simplified analysis within the standard quasispecies formalism. While we obtained a selective advantage for sexual replication using this mating strategy, a fuller analysis will require the consideration of various mating strategies on the selective advantage for sex. An important such mating strategy, which is the opposite of the one considered in this paper, is the random mating strategy, whereby all haploids are capable of engaging in sexual recombination, and do so with a pairwise distribution given by the Hardy-Weinberg equilibrium.

In this vein, one interesting question is to determine, for a given fitness landscape, whether there always exists a mating strategy for which sexual replication will outcompete asexual replication. Additionally, while this paper implicitly assumed that the strategy for sexual or asexual replication is inherited, future studies should consider genomes where genes for sex are explicitly included. This leads to the ability for sexual organisms to mutate into asexual ones. As the selective advantage for sexual replication disappears (as a function of mutation rate, for instance), the models may exhibit localization to delocalization transitions over the portions of the genome controlling sex.

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